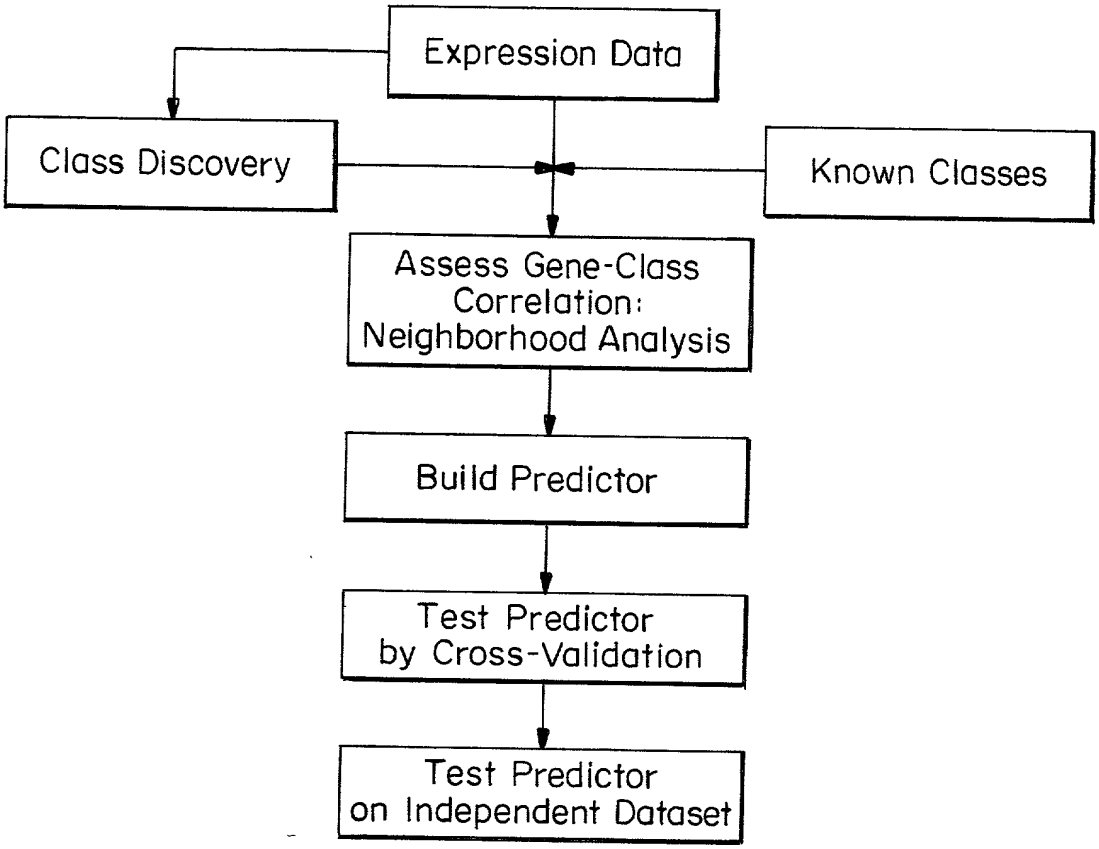

Expression Data
Class Discovery
Known Classes
Assess Gene-Class Correlation: Neighborhood Analysis
Build Predictor
Test Predictor by Cross-Validation
Test Predictor on Independent Dataset

FIG. 1A

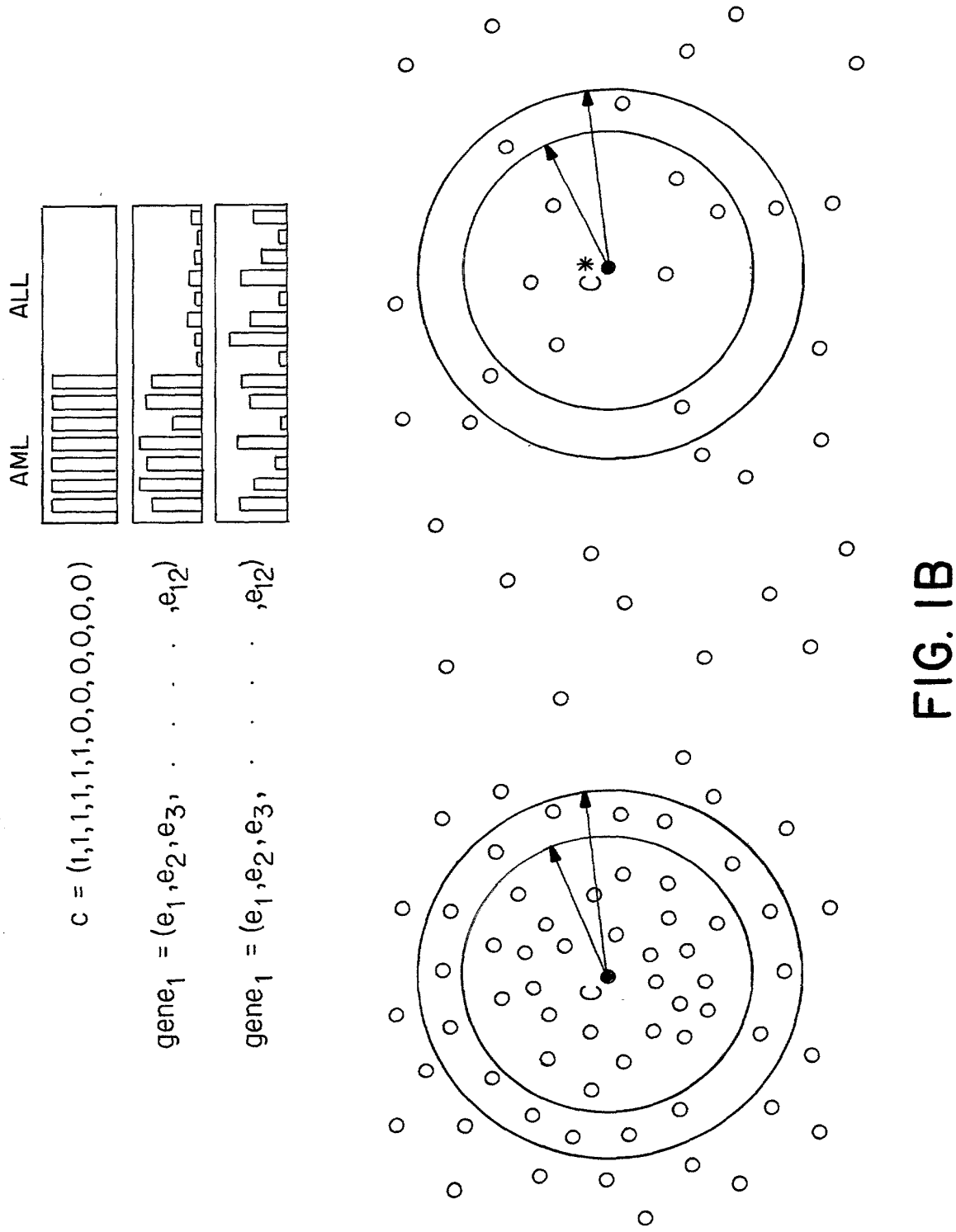


FIG. 1B

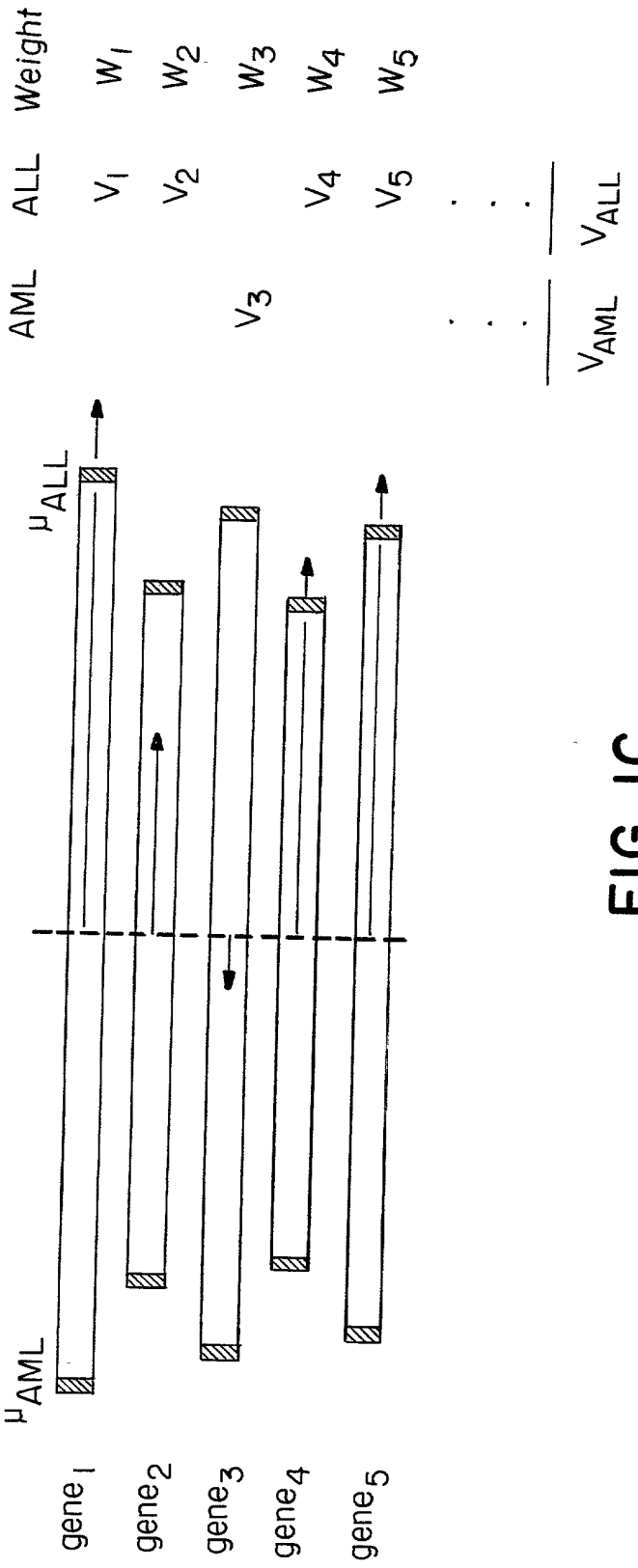

Weight
ALL
AML
W_1
W_2
W_3
W_4
W_5
V_1
V_2
V_3
V_4
V_5
V_{ALL}
V_{AML}
μ_{ALL}
μ_{AML}
gene 1
gene 2
gene 3
gene 4
gene 5

FIG. 1C

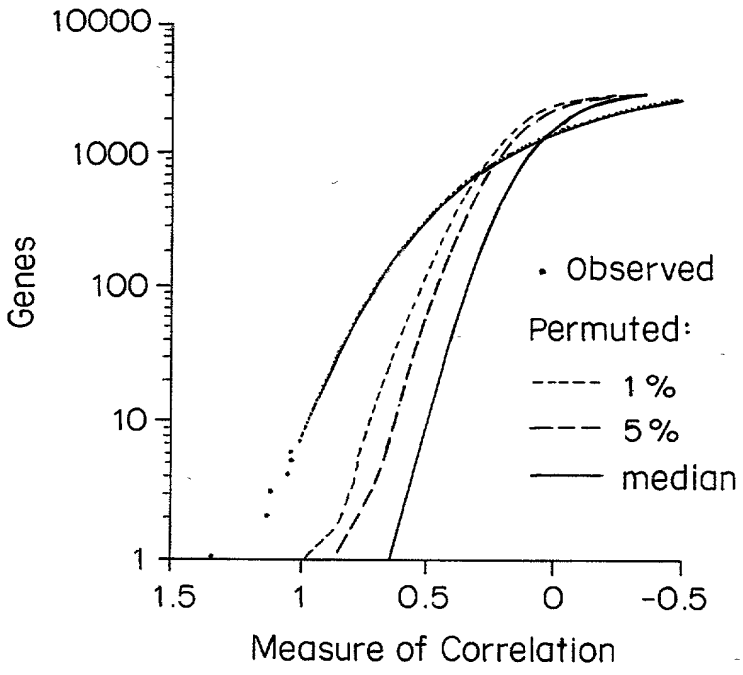

10000
1000
100
10
1
Genes
1.5
1
0.5
0
-0.5
Measure of Correlation
• Observed
Permuted:
----- 1%
--- 5%
—— median

FIG. 2A

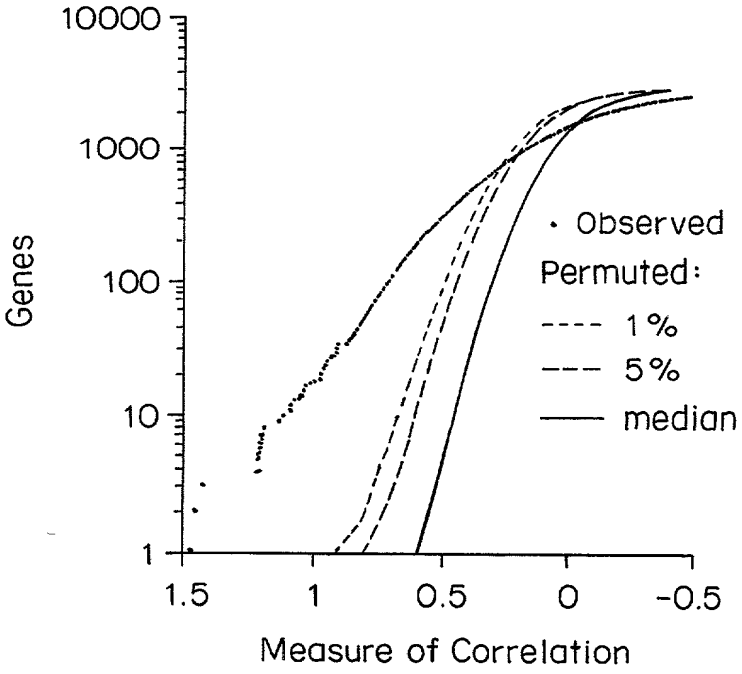

10000
1000
100
10
1
Genes
1.5
1
0.5
0
-0.5
Measure of Correlation
• Observed
Permuted:
---- 1%
--- 5%
—— median

FIG. 2B

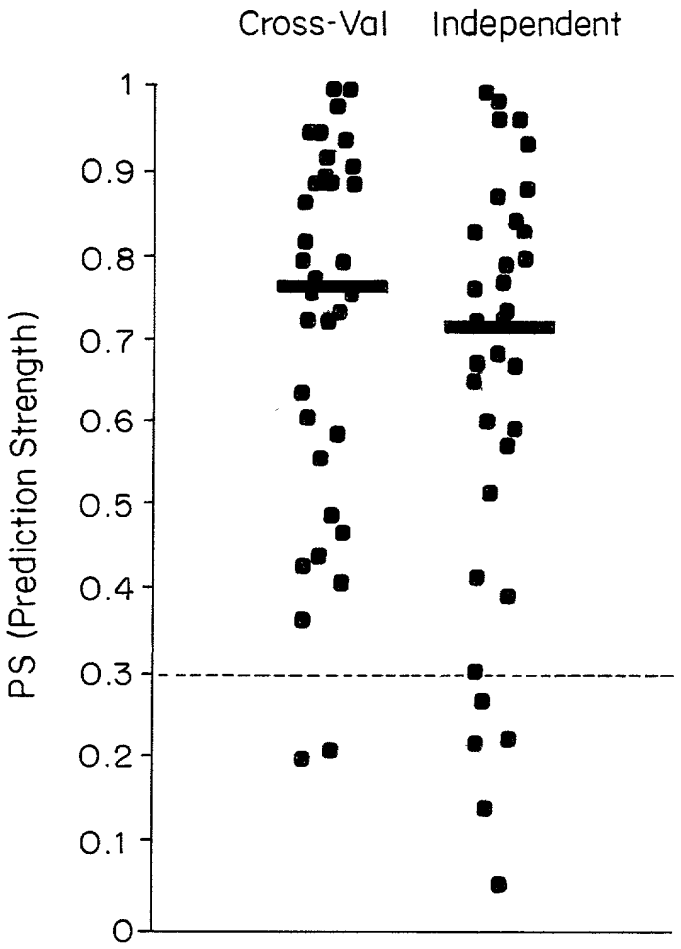

Cross-Val
Independent
PS (Prediction Strength)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0

FIG. 3A

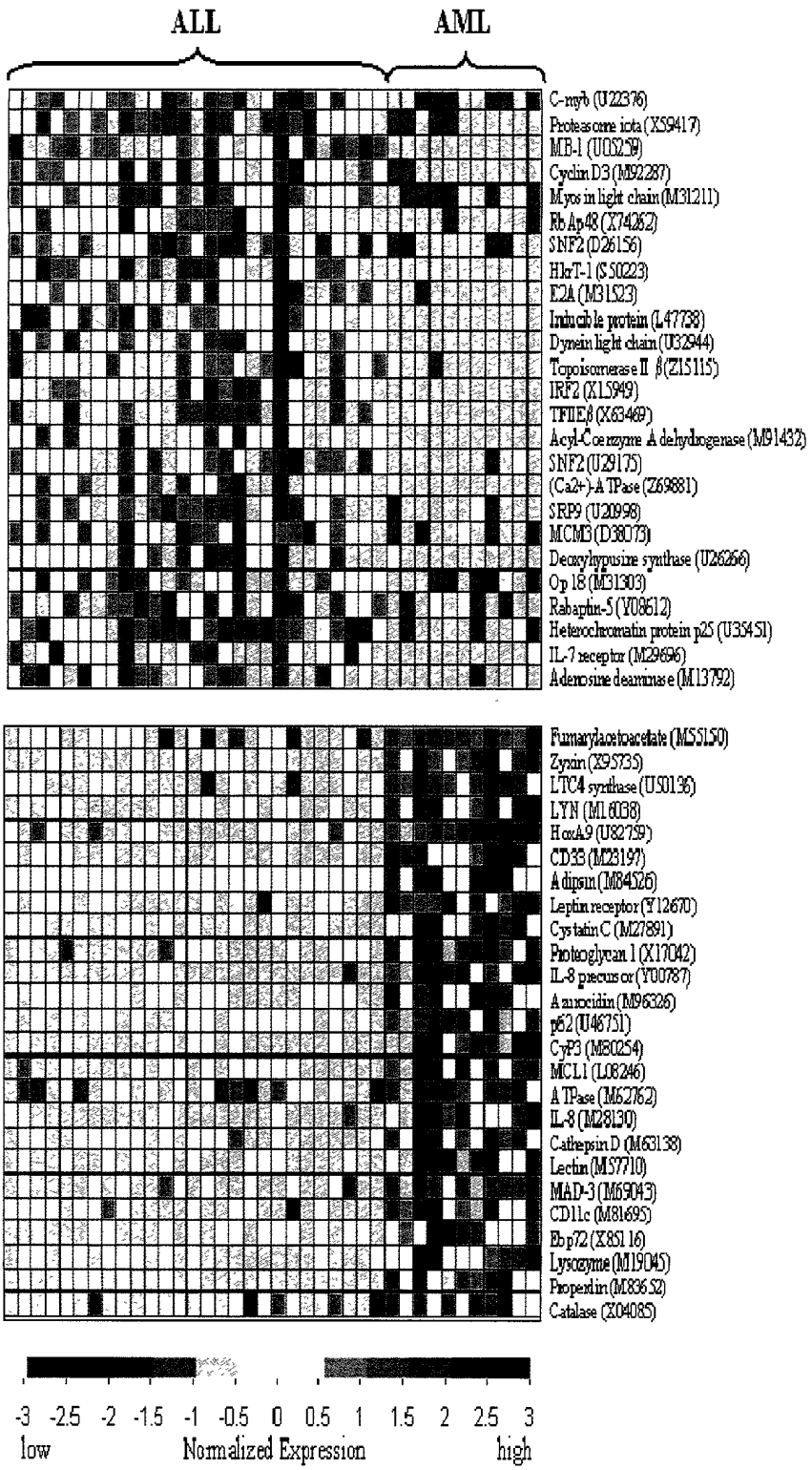

ALL
AML
C-myb (U22376)
Proteasome iota (X59417)
MB-1 (U05259)
Cyclin D3 (M92287)
Myosin light chain (M31211)
RbAp48 (X74262)
SNF2 (D26156)
HlaT-1 (S50223)
E2A (M31523)
Inducible protein (L47738)
Dynein light chain (U32944)
Topoisomerase II β (Z15115)
IRF2 (X15949)
TFIIEβ (X63469)
Acyl-Coenzyme A dehydrogenase (M91432)
SNF2 (U29175)
(Ca2+)-ATPase (Z69881)
SRP9 (U20998)
MCM3 (D38073)
Deoxyhypusine synthase (U26266)
Op 18 (M31303)
Rabaptin-5 (Y08612)
Heterochromatin protein p25 (U35451)
IL-7 receptor (M29696)
Adenosine deaminase (M13792)
Fumarylacetoacetate (M55150)
Zyxin (X95735)
LTC4 synthase (U50136)
LYN (M16038)
HoxA9 (U82759)
CD33 (M23197)
Adipsin (M84526)
Leptin receptor (Y12670)
Cystatin C (M27891)
Proteoglycan 1 (X17042)
IL-8 precursor (Y00787)
Azurocidin (M96326)
p62 (U46751)
CyP3 (M80254)
MCL1 (L08246)
ATPase (M62762)
IL-8 (M28130)
Cathepsin D (M63138)
Lectin (M57710)
MAD-3 (M69043)
CD11c (M81695)
Ebp72 (X85116)
Lysozyme (M19045)
Properdin (M83652)
Catalase (X04085)
-3 -2.5 -2 -1.5 -1 -0.5 0 0.5 1 1.5 2 2.5 3
low
Normalized Expression
high

FIG. 3B

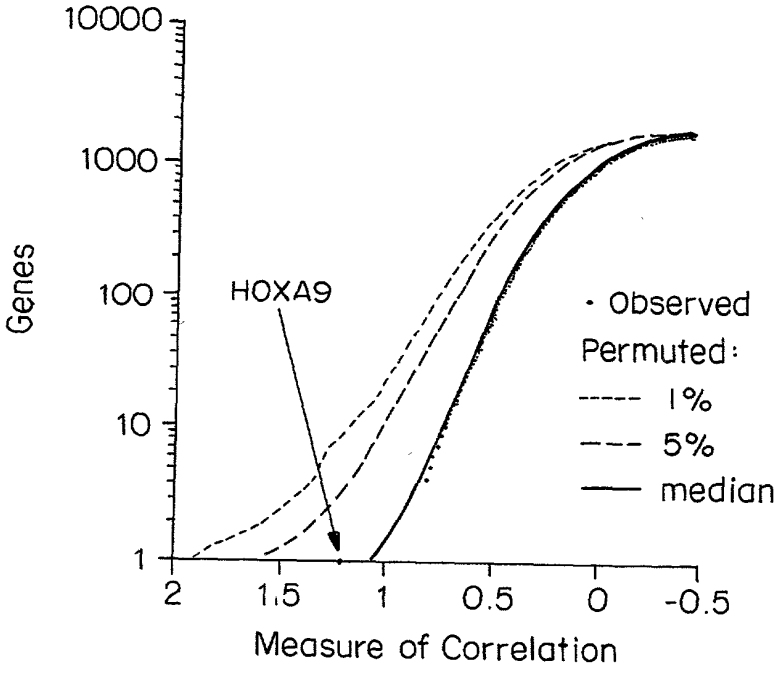

10000
1000
100
10
1
Genes
HOXA9
· Observed
Permuted:
1%
5%
median
2
1.5
1
0.5
0
-0.5
Measure of Correlation

FIG. 4A

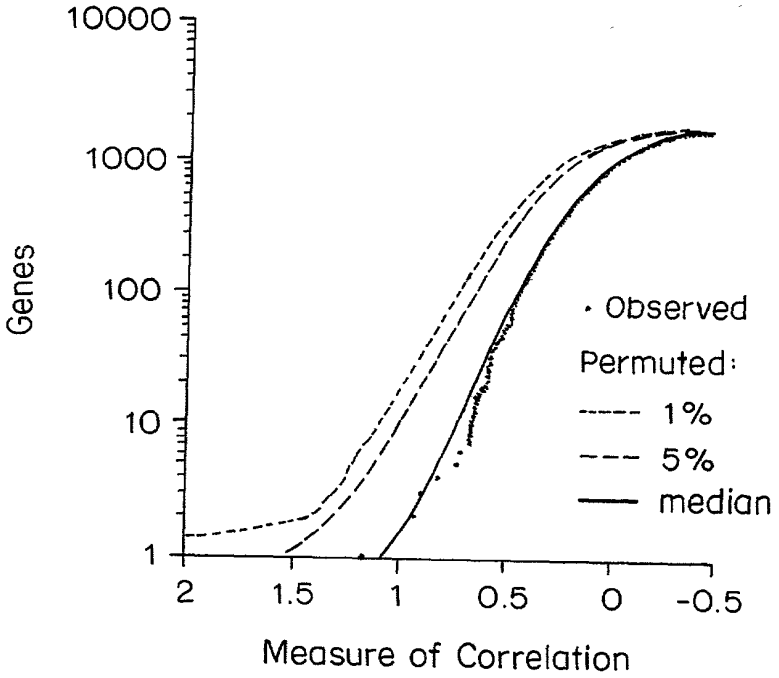

10000
1000
100
10
1
Genes
· Observed
Permuted:
1%
5%
median
2
1.5
1
0.5
0
-0.5
Measure of Correlation

FIG. 4B

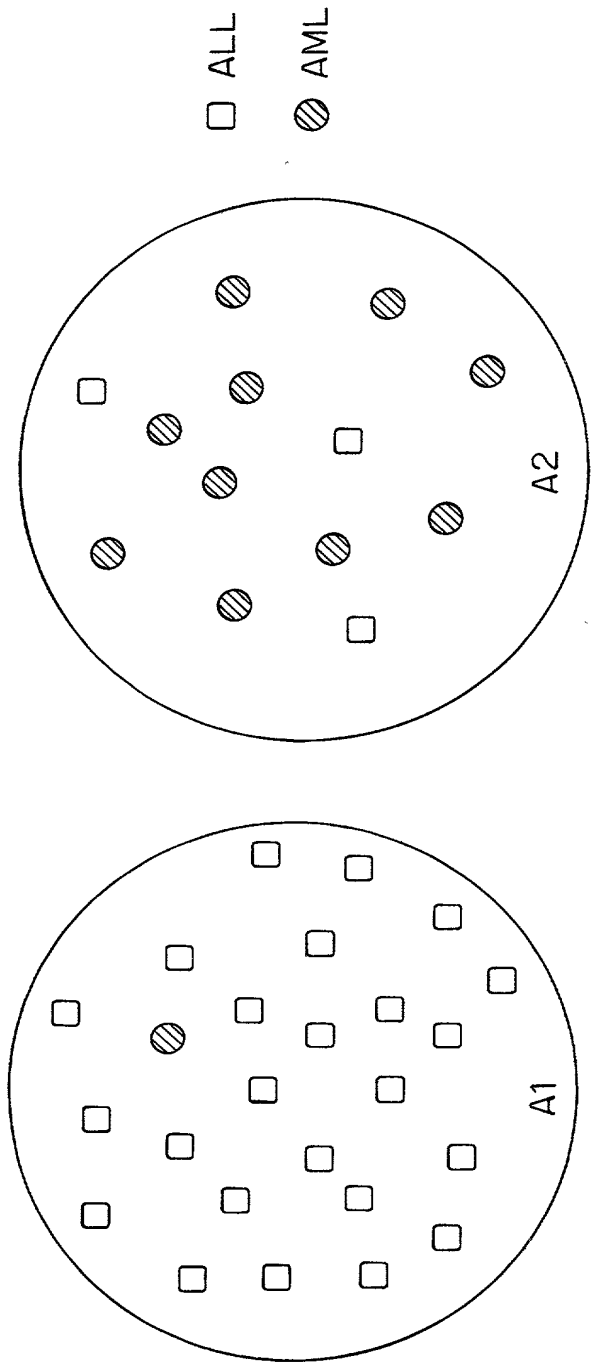


FIG. 5A

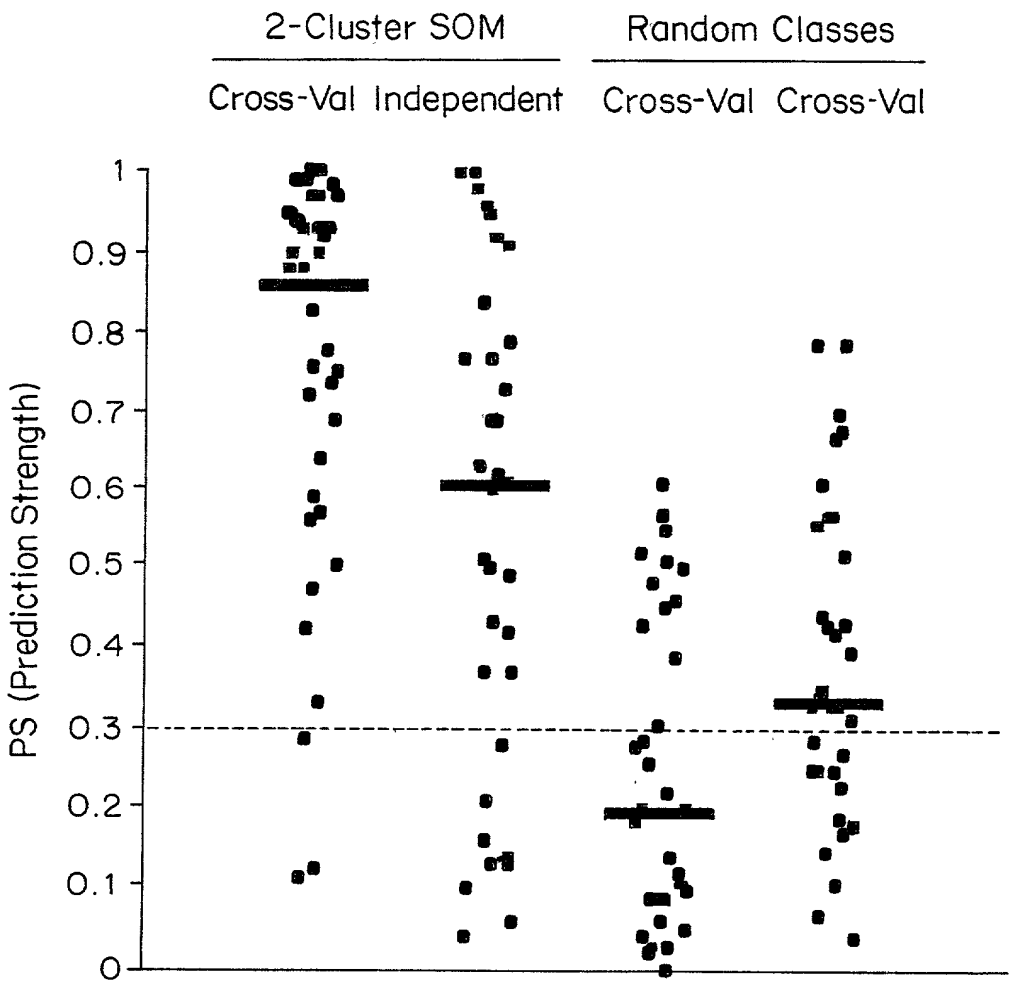


FIG. 5B

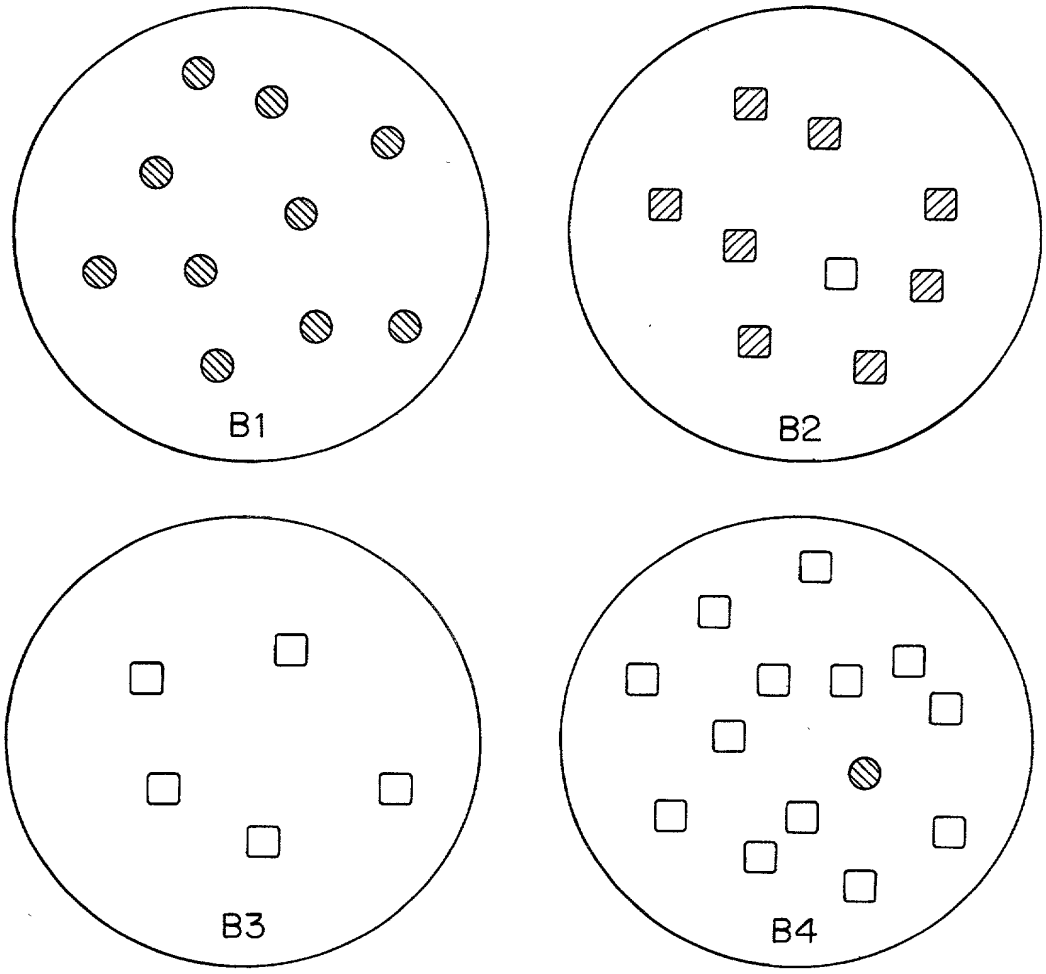


FIG. 5C

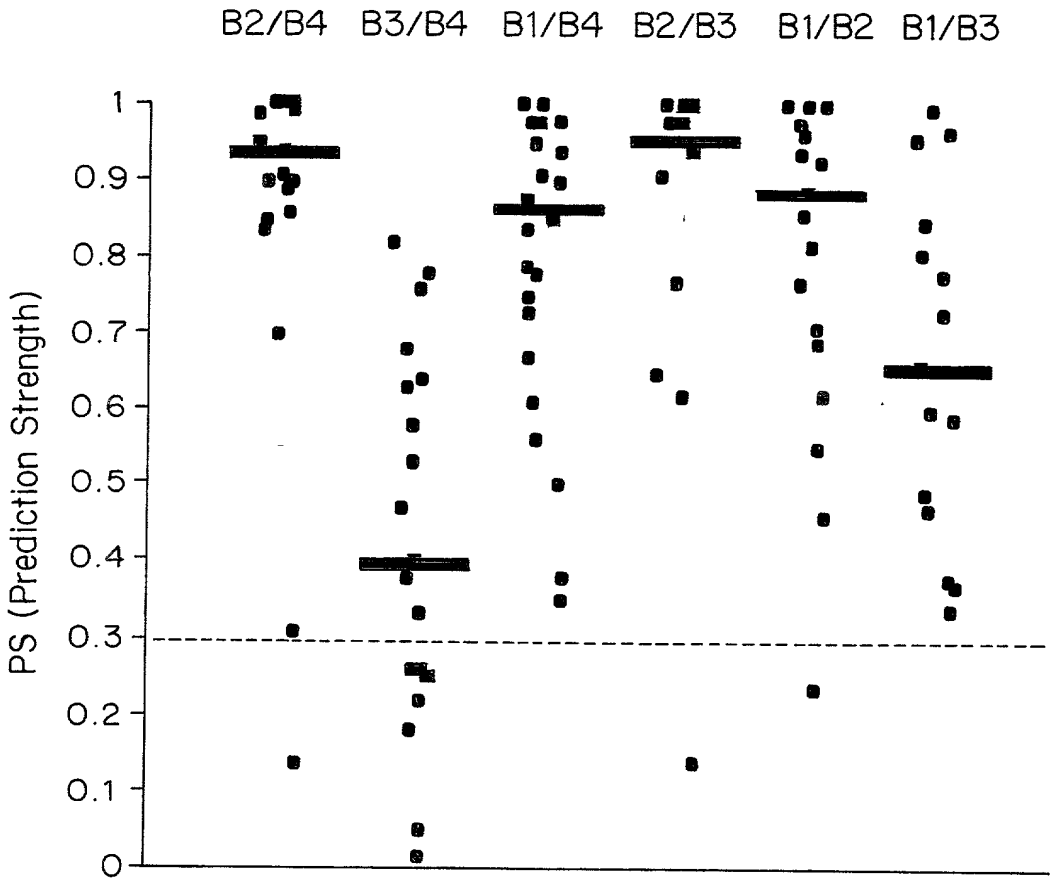

B2/B4
B3/B4
B1/B4
B2/B3
B1/B2
B1/B3
PS (Prediction Strength)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0

FIG. 5D

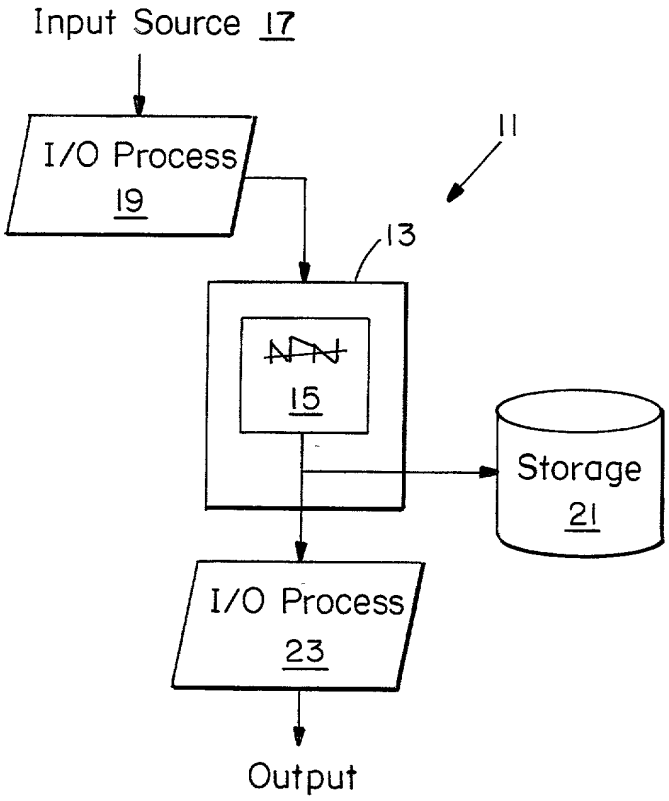

Input Source 17
I/O Process
19
11
13
15
Storage
21
I/O Process
23
Output

FIG. 6

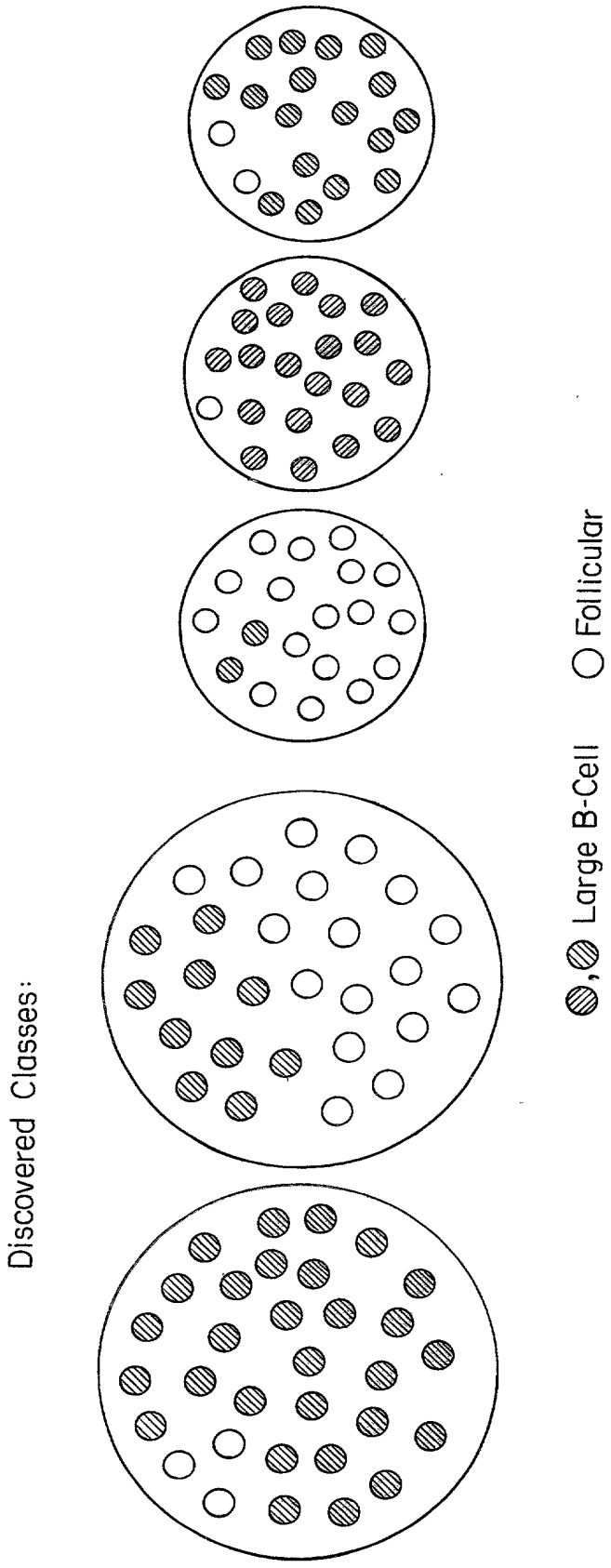


FIG. 7

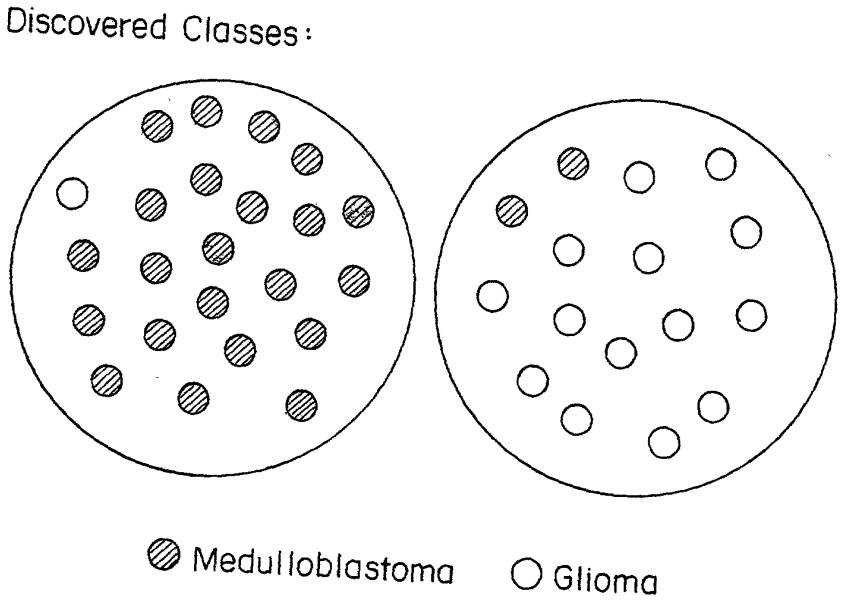


FIG. 8

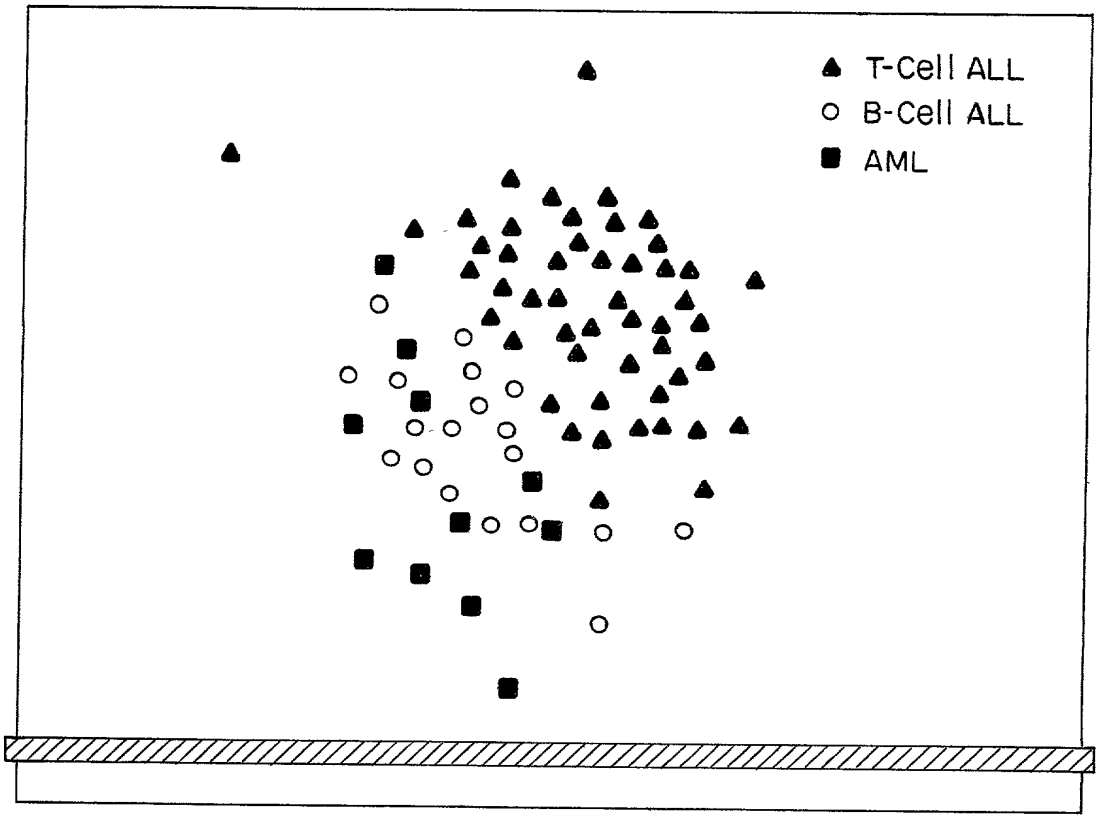
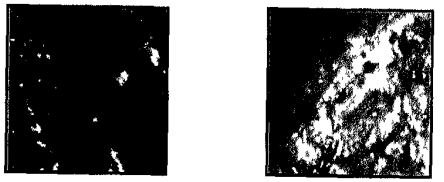
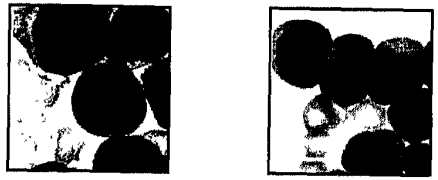
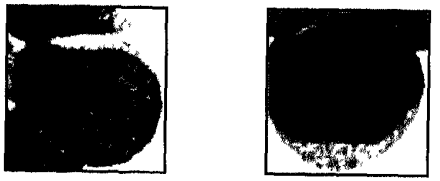
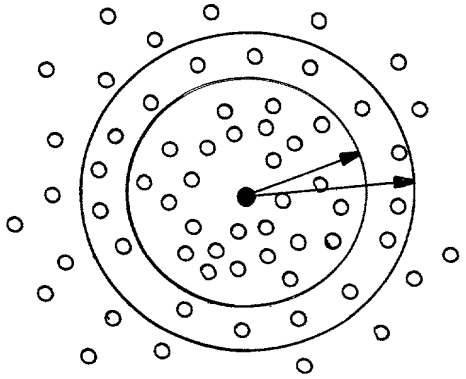


FIG. 9

FIG. 10

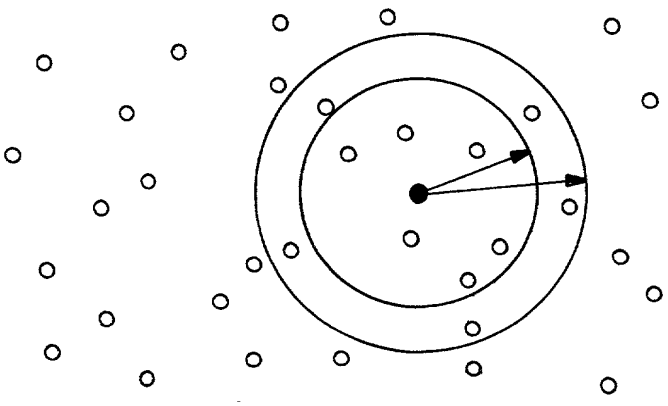
Hierarchy of Problems in Molecular Class Prediction

Problem:	Difficulty:	Gene Markers:	Error:	Example:
I. Tissue or Cell Type Normal vs. Abnormal	Low	~1000-2000	~0%	Normal vs. Renal Carcinoma 
II. Morphological Type	Low-medium	~200-500	~0-5%	Leukemia ALL vs. AML 
III. Morphological Subtype	Medium-high	~50-100	~0-15%	ALL B- vs. T-Cell 
IV. Treatment Outcome Drug Sensitivity	High	~1-20	~5-50%	AML Treatment Outcome 



Class Pattern
Neighborhood

FIG. 11A



Permuted Pattern
Neighborhood

FIG. 11B

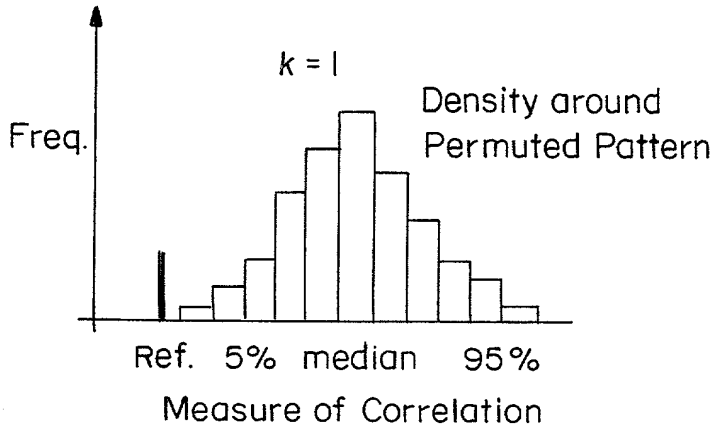


FIG. 11C

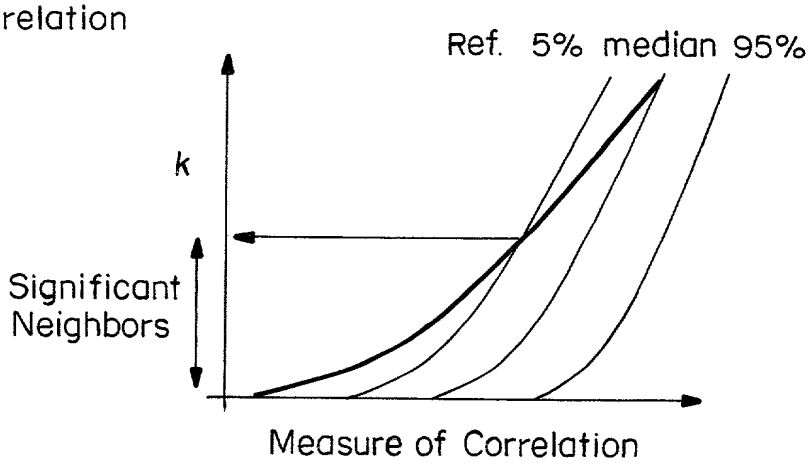


FIG. 11D

CLASS PREDICTION RESULTS

Problem Type	Biological System	Problem Distinction	Number of samples	Number of errors	Number of no calls	Number of errors (all calls)	Number of gene markers
I	Renal	Normal v. Carcinoma	12	0 (0%)	0	0 (0%)	>100
II	Leukemia	ALL vs AML	35	0 (0%)	2	0 (0%)	700
III	Leukemia	ALL B v. T-Cell	33	0 (0%)	1	1 (3%)	200
IV	Leukemia	Treatment Outcome	15	2 (13%)	0	2 (13%)	1

Fig. 12